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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	18

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N.	Applicant(s)
	09/844684	MIKAYAMA
	Examiner	Art Unit
	GAMBEL	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 3/24/03, 1/7/03, 12/16/02

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) ____ is/are pending in the application. 3-6, 8, 10-13, 15, 17, 18, 20, 22-26, 30-61, 65, 66

4a) Of the above claim(s) ____ is/are withdrawn from consideration.

5)☑ Claim(s) 66 is/are allowed. → 30-61

6)☑ Claim(s) ____ is/are rejected. → 3-6, 8, 10-13, 15, 17, 18, 20, 22-26, 65

7)☐ Claim(s) ____ is/are objected to.

8)☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☑ The drawing(s) filed on ____ is/are: a)☑ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on ____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. ____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☑ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☑ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
4)☐ Interview Summary (PTO-413) Paper No(s). ____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Applicant's amendment, filed 3/24/03 (Paper No. 16), has been entered.
Claims 1, 7, 14, 16, 19, 21, 27, 28, 29, 62, 63 and 64 have been canceled.
Claims 2 and 9 have been canceled previously.

Claims 65-66 have been added.

Claims 3-12, 15, 17, 18, 20 and 22-25 have been amended.

Claims 3-6, 8, 10-13, 15, 17, 18, 20, 22-26, 30-61, 65 and 66 are pending.

2. Applicant's election of Group I in Paper No. 13 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 30-61 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to nonelected inventions.

Claims 3-6, 8, 10-13, 15, 17, 18, 20, 22-26, 65 and 66 are under consideration in the instant application.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It does not identify the mailing or post office address of each inventor. A mailing or post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing or post office address should include the ZIP Code designation. The mailing or post office address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

4. Formal drawings, filed 12/16/02, comply with 37 CFR 1.84.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected. Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required.

6. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 3-6, 8, 10-13, 15, 17, 18, 20, 22-26 and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

It is apparent that number 11, 72, F1-102, F4-465, F2-103, F5-77, F5-157 antibodies and associated hybridomas are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the pertinent hybridomas which produce these antibodies. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

8. Claims 25-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "an nucleic acids that encodes the antibodies and host cells that express said nucleic acids produced by the specific hybridomas set forth in claim 3 (and recited in claims 4-5), does not reasonably provide enablement for any "nucleic acid encoding any human monoclonal antibody wherein the antibody has CD40 binding specificity / CD40 modulating activity of the specific antibodies / hybridomas recited in claims 4-5.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has not provided sufficient biochemical information (e.g. sequence information or provided the hybridomas) of any antibody has the CD40 binding specificity / CD40 modulating activity of these specific antibodies / hybridomas that distinctly identifies such antibodies having CD40 binding specificity / CD40 modulating activity that enables the skilled artisan to obtain the claimed nucleic acids encompassed by the claimed invention.

For examination purposes, claim 3 and dependent claims thereof read on the specific antibodies / hybridomas recited in claim 3.

Claims 4-5 are broader in reading on antibodies and fragments thereof the CD40 binding specificity / CD40 modulating activity of these specific antibodies / hybridomas. In turn, the claims read on a broader range of nucleic acids encoding said antibodies and fragments thereof.

Given the well known polymorphism of immunoglobulins / antibodies; it would have been undue experimentation to derive the vast repertoire of nucleic acids resulting from somatic recombination and hypermutation mutation encoding nucleic acids encoding such antibodies having CD40 binding specificity / CD40 modulating activity of the specific antibodies / hybridomas recited in claims 3-5, commensurate in scope with the claimed invention.

Without sufficient guidance and given the well known polymorphism of immunoglobulins / antibodies; it would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue to determine the vast repertoire of nucleic acids such antibodies having CD40 binding specificity / CD40 modulating activity of the specific antibodies / hybridomas recited in claims 3-5.

9. Claims 25-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification broadly describes and the claims recite as part of the invention nucleic acids encoding any human monoclonal antibody wherein the antibody has CD40 binding specificity / CD40 modulating activity of the specific antibodies / hybridomas recited in claims 4-5. The specification does not describe any nucleic acid encoding human monoclonal antibody wherein the antibody has CD40 binding specificity / CD40 modulating activity of the specific antibodies / hybridomas recited in claims 4-5, broadly encompassed by the claimed invention.

Given the well known polymorphism of immunoglobulins / antibodies; it would have been undue experimentation to derive the vast repertoire of nucleic acids resulting from somatic recombination and hypermutation mutation encoding nucleic acids encoding antibody has CD40 binding specificity / CD40 modulating activity of the specific antibodies / hybridomas recited in claims 4-5, commensurate in scope with the claimed invention. Applicant was not in possession of the structural attributes of a representative number of species possessed by the members of the genus of "nucleic acids encoding antibody has CD40 binding specificity / CD40 modulating activity of the specific antibodies / hybridomas recited in claims 4-5, encompassed by the claimed invention.

Such sequences do not meet the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Such isolated nucleic acids encoding the specific antibodies / hybridomas recited in claims 3-5 meet the written description provision of 35 USC 112, first paragraph.

The specification as filed does not provide written description support for any nucleic acid encoding any antibody has CD40 binding specificity / CD40 modulating activity of the specific antibodies / hybridomas recited in claims 4-5. The skilled artisan cannot envision all the contemplated nucleotide sequences by the detailed chemical structure of the claimed polynucleotides and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Again, in the instant case; the specification provides only written description for nucleic acids and appropriate host cells consisting of the particular antibodies / hybridomas produced by the particular hybridomas recited in claims 3-5; but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. Claims 5, 6, 8, 10 and 23-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 5, 6, 8, 10 and 23-26 are indefinite in its recitation of "modulating" because it is ambiguous as to the nature, direction (positive or negative) or degree of said modulating. The recitation of "modulating" is a relative term which renders the claims indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

B) Claim 23 is indefinite in that in it depends on a compound claim, yet recites a composition claim. Therefore, the claims lacks proper antecedent basis.

C) Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 4, 5, 6, 11, 18, 20 and 22-26 are rejected under 35 U.S.C. § 102(e) as being anticipated by Kucherlapati et al. (U.S. Patent No. 6,150,584) (see entire document) alone and in further evidence by de Boer (U.S. Patent No. 5,874,082).

Kucherlapati et al. teach human antibodies derived from immunized xenomice, including antibodies directed towards leukocyte markers such as CD40 (see column 9, paragraph 5, particularly column 9, line 60). Kucherlapati et al. also teach immunoglobulin analogs such as $F(ab')_2$, Fab', Fab and single chain Fv (see column 4, paragraph 4). Kusherlapati et al. teach immunoglobulin encoding nucleic acids and cells (e.g. hybridomas) containing said human antibodies and nucleic acids encoding said antibodies (see Detailed Description, including Examples).

For examination purposes, human monoclonal antibody wherein the antibody has CD40 binding specificity of the specific antibodies / hybridomas recited in claims 4 read on human antibodies that bind CD40 and not on anti-CD40 antibodies that bind any particular epitope.

De Boer disclose that all anti-CD40 known in the art have a stimulatory effect on B cells (column 2, paragraph 3). For examination purposes, human monoclonal antibody wherein the antibody has CD40 modulating activity of the specific antibodies / hybridomas recited in claim 5 read on agonistic human antibodies that bind CD40 and not on agonistic anti-CD40 antibodies that bind any particular epitope.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations of binding and agonistic anti-CD40 antibodies (e.g. claims 11, 18, 22) would be inherent properties of the referenced human anti-CD40 antibodies. A composition is a composition irrespective of what its intended use is. Given the well known usage of lambda sequences, the claimed structural property of the human monoclonal antibody containing a lambda light chain sequence would have been an inherent property of the referenced human anti-CD40 antibodies.

14. Claims 4-6, 8, 10-13, 15, 17, 18, 20 and 22-26 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kucherlapati et al. (U.S. Patent No. 6,150,584) in view of de Boer (U.S. Patent No. 5,874,082).

Kucherlapati et al. teach human antibodies derived from immunized xenomice for various therapeutic modalities (see entire document), including antibodies directed towards leukocyte markers such as CD40 (see column 9, paragraph 5, particularly column 9, line 60). Kucherlapati et al. also teach immunoglobulin analogs such as $F(ab')_2$, Fab', Fab and single chain Fv (see column 4, paragraph 4). In addition, Kusherlapati et al. teach immunoglobulin encoding nucleic acids and cells (e.g. hybridomas) containing said human antibodies and nucleic acids encoding said antibodies (see Detailed Description, including Examples).

Kucherlapati et al. differs from the claimed invention by not disclosing the specific antibodies / hybridomas recited in claims 4-5.

Kucherlapati et al. differs from the claimed invention by not exemplifying the agonistic and antagonistic human anti-CD40 antibodies

De Boer et all. teach both agonistic and antagonistic anti-CD40 antibodies (see entire document). De Boer disclose that all anti-CD40 known in the art have a stimulatory effect on B cells (column 2, paragraph 3) and teach antagonistic anti-CD40 antibodies (see Summary of the Invention, Detailed Description of the Invention and Claims). De Boer et al. teach that antibodies and labeled antibodies can be used for a variety of procedures (see Detailed Description). De Boer et al. teach a variety of assays to test anti-CD40 antibodies (see entire document) and that CD40 epitopes can be identified (see column 7, paragraph 4 - column 8, paragraph 2).

Given the properties of both agonistic and antagonistic anti-CD40 antibodies, including a number of binding and functional assays taught by De Boer, the claimed binding and functional properties of human anti-CD40 antibodies (e.g. claims 11, 12, , 17, 18, 22)would have expected properties associated with said agonistic and antagonistic anti-CD40 antibodies by the ordinary artisan at the time the invention was made.

For examination purposes, human monoclonal antibody wherein the antibody has CD40 binding specificity of the specific antibodies / hybridomas recited in claims 4 read on human antibodies that bind CD40 and not on anti-CD40 antibodies that bind any particular epitope.

For examination purposes, human monoclonal antibody wherein the antibody has CD40 modulating activity of the specific antibodies / hybridomas recited in claim 5 read on agonistic human antibodies that bind CD40 and not on agonistic anti-CD40 antibodies that bind any particular epitope.

One of ordinary skill in the art at the time the invention was made would have been motivated to select CD40 as a target for both agonistic and antagonistic human monoclonal antibodies for a variety of assays and therapeutic modalities. The ordinary artisan was motivated to select human monoclonal antibodies, given their decreased immunogenicity in humans. One would have been motivated to select for antibodies having different functional activities (e.g. agonistic and antagonistic) in view of the teaching of De Boer that antibodies having different biological characteristics were recognized to be useful for structural and functional studies as well as targeting and therapeutic modalities at the time the invention was made. The usefulness of monoclonal antibodies with respect to their specificity of binding, their homogeneity and their ability to be produced in unlimited quantities was well known in the art at the time the invention was made. In addition, antibodies were routinely used for purification and detection assays as well as a number of in vitro and in vivo functional assays and procedures. Given the well known usage of lambda sequences, the claimed structural property of the human monoclonal antibody containing a lambda light chain sequence would have been an expected property of the referenced human anti-CD40 antibodies. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claim 66 is allowed.

Due to high polymorphism of antibodies, the specific antibodies set forth in claim 3 and their respective hybridomas are deemed structurally distinct on the primary amino acid basis and therefore free from the prior art.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
June 13, 2003